DAC #18

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

SERIAL NO.:	08/765,695	§	DOCKET NO. P-01525US0
		§	
FILING DATE:	JULY 25, 1997	§	EXAMINER:
		§	R. SCHWADRON
APPLICANT:	LARS ABRAHMSEN, ET AL.	§	
		§	
TITLE:	"CONJUGATE BETWEEN A MODIFIED SUPERANTIGEN AND A TARGET-SEEKING COMPOUND AND THE USE OF THE CONJUGATE"	§	GR ART UNIT 1644

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

PETITION TO THE COMMISSIONER UNDER 37 C.F.R. § 1.181 FROM IMPROPER REQUIREMENT FOR RESTRICTION

Applicants respectfully Petition the Commissioner under the provisions of 37 C.F.R. § 1.144 and 1.181 for withdrawal of an improper requirement for restriction pending in the above-referenced case.

As explained below, the Examiner is maintaining the requirement on the ground that, allegedly, the independent claims of the case as filed are not patentable over the prior art (Buelow

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231 on 11-15-99
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Linda Bourg (Signature) 11-15-99 (Date)

et al., in particular) and therefore restriction is proper under MPEP Section 1850 (July 1998, 1800-51). Applicants assert that all the independent claims as filed are patentable over the prior art, therefore unity of invention is present, and the restriction requirement should be withdrawn.

Statement of Facts

The above-captioned patent application bears a United States Patent and Trademark Office filing date of July 25, 1997. Claims 14-51 were initially pending. On October 16, 1998 a Restriction Requirement was issued which defined Group I claims (14-35) as being drawn to a conjugate and Group II claims (36-51) as being drawn to a method of treatment using the conjugate. The independent claims as filed are:

Group I:

14. A conjugate comprising:

a. a biospecific affinity counterpart that is capable of binding to a surface structure, and

b. a peptide that

i. contains an amino acid sequence that is derived from a superantigen,

ii. has the ability to bind to a Vβ of a T cell receptor, and

iii. has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived,

which parts are covalently linked together.

Group II:

36. A method for the treatment of a diseased condition in a mammal, which condition means the presence of specific cells that are associated with the condition by the expression of a disease specific cell surface structure, wherein one administers to the mammal a therapeutically effective amount of covalent conjugate that is able to activate T lymphocytes to lyse cells that carry the disease specific cell surface structure and comprises:

a. a biospecific affinity counterpart that is capable of binding to said surface structure, and

b. a peptide that

i. contains an amino acid sequence that is derived from a superantigen,

ii. has the ability to bind to a Vβ of a T cell receptor, and

iii. has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived.

The restriction requirement was based upon the Examiner's assertion that the special technical linking feature of the groups, the conjugate of Group I, was allegedly not patentable over Buelow et al. (J. Immunol., 1992, 148:1-6).

On November 16, 1998 applicants responded to the restriction requirement with traverse, provisionally electing claims of Group II. Reconsideration of the restriction requirement was requested.

On August 16, 1999 a first substantive Office Action was issued on the case. (Applicants note with concern that the first substantive examination in the case was not issued until more than two years following the U.S. filing date of the application). In that Office Action the Examiner maintained and made Final the restriction requirement based upon the same grounds, the alleged unpatentability of the independent claims over Buelow.

Point For Review

Applicants respectfully submit that the restriction requirement is improper because the independent claims are patentable over the prior art and thus all claims as filed should be examined in a single application as required under PCT Article 3(4)(iii) and 17(3)(a), PCT Rule 3.1, 37 C.F.R. § 1.475, and MPEP Section 1850.

Arguments

The Examiner is basing this Restriction Requirement upon the position that the independent claims are allegedly not patentable over Buelow, et al., J. Immunol., 1992, 148:1-6. The is incorrect because the Examiner's position is based upon an incorrect interpretation of Buelow.

The Examiner is basing the unpatentability rejection on the following assertion (emphasis added):

> Buelow et al. teach a protein A-SEB conjugate wherein the SEB of the conjugate only contains amino acids 1-130 of SEB (see Figure 4)...[t]his conjugate can bind the VB of a TCR (because it stimulates T cells, see Figure 4)...It is an inherent property of said mutated conjugate that it has a modified ability to bind MHC class II antigens because it lacks SEB residues important for class II binding (e.g., such as residue 227, see specification, pages 22-23).

This statement is incorrect. The SEB conjugate of Buelow that contains amino acids 1-130 of SEB does not stimulate T cells. As shown in Buelow in Figure 4 and, for example, also on page 5, left column, "[t]he pCA-SEB fusion protein with residues 131-239 at the carboxy terminus deleted [i.e., SEB with amino acids 1-130] had neither mitogenic nor tolerogenic activity."(emphasis added).

Furthermore, Buelow does not in any manner teach, disclose or suggest modifying residues in a full length superantigen in order to affect MHC Class II antigen binding. It is entirely unclear from Buelow which regions of a full length superantigen should be mutated in order to expect a mutant protein with altered MHC Class II binding. The disclosure, teaching and suggestion of Buelow all are directed solely to the *use of truncated pCA-SEB fusion proteins to map to the amino-terminal half of the molecule (residues 1-138) a minimally immunologically active domain of SEB capable of inducing proliferation and anergy in cloned human T cells expressing VB3.1* (see first paragraph of page 2, Buelow). Buelow is not aimed at identifying the MHC Class II binding domain

and certainly is not aimed at identifying which residues of full length superantigens may be mutated to specifically alter Class II MHC antigen binding. Buelow provides an indication that the region encompassing residues 1-138 of SEB constitutes a functional (i.e., "immunologically active") domain of the molecule; however, the Buelow authors recognize that it remains to be determined which parts of the molecule are involved in the interactions with Class II MHC antigens and TCR molecules, for example, directly, and/or indirectly (for example by influencing the conformation of the molecule) (see Discussion section on page 6, Buelow).

Indeed, the actual data presented in Buelow makes it clear that it does not teach or predict anything about Class II MHC antigen binding. For example, F45 and E67 are known to be important for Class II MHC binding in SEB and both the Buelow 1-130 and 1-138 SEB fragments have these identical (wild-type) sequences. However, as discussed above and plainly shown in Buelow, these two proteins have dramatically differing activities; the fragment 1-130 has neither mitogenic nor tolerogenic activity, while 1-138 fragment (identical *but for* the additional eight amino acids which are not in the recognized Class II MHC binding region) has activity. Hence, there is no way that one skilled in the art could gain any information from Buelow about which residues in superantigens are important in Class II MHC binding.

Applicants, therefore, respectfully assert that all claims as originally presented and currently pending (claims 14-38, 44-47 and 52-57) are patentable as a single invention.

Action Requested

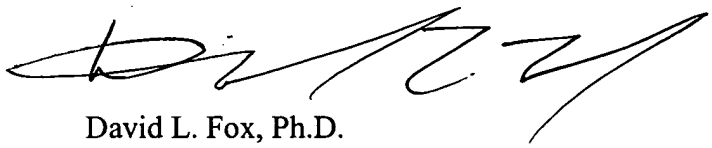
In light of the above-noted facts, and arguments, applicants respectfully request that the presently pending restriction requirement be withdrawn and all claims as filed and presently pending (claims 14-38, 44-47 and 52-57) be examined on the merits in the above-noted patent application.

Fees Paid

Please charge any fees due for this Petition to the standing account of Fulbright & Jaworski L.L.P., Deposit No. 06-2375 under Order No. 984877.

Applicants respectfully petition for any extension of time necessary to render this response timely.

Respectfully submitted,



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